Remarks

References to hyperlinks in the specification have been removed, overcoming the objection to the specification.

Claims withdrawn from further consideration as drawn to a nonelected invention have been canceled (Claims 1-24 and 33-42).

Claims 25-28 have been amended. Support for the length of the oligonucleotide is found at page 10, lines 18-19, of the specification. Disclosure of the percent homology being related to a defined length of the two molecules being compared, and at least about 95% homology, is found at page 14, lines 17-20. An oligonucleotide comprising at least 8 contiguous nucleobases of the recited sequences is disclosed at page 22, lines 8-12. The term "specifically hybridizable" in Claim 26 is defined at page 11, lines 9-12. .

Rejection Under 35 USC §112, Second Paragraph

Claims 25-32 are rejected under 35 USC §112, second paragraph, as allegedly indefinite for failing to make clear whether the isolated oligonucleotide or the contiguous nucleobases is/are substantially identical or complementary to at least a portion of SEQ ID NO: 21 or an RNA sequence corresponding thereto. The present amendments to Claim 25 clarify that the isolated oligonucleotide is at least about 95% homologous over its full length to any of eight specific sequences or corresponding RNAs. Reference to substantial identity or complementarity to "at least a portion" of the sequence has been deleted. Applicants submit that the claims as amended are definite and withdrawal of the rejection is requested.

Rejection Under 35 USC §102(b)

Claims 25-28 and 32 are rejected under 35 USC §102(b) as allegedly anticipated by Koster et al. (US Patent No. 6,043,031, hereinafter "'031"). The Examiner notes that SEQ ID NO: 2 of '031

contains an 8 nucleobase portion that is complementary to SEQ ID NO: 17, SEQ ID NO: 21 and SEQ ID NO: 32 of the instant invention. The amended claims delete the recitation of "complementary" but require that the isolated oligonucleotide comprises 8 contiguous nucleobases of SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34 or an RNA sequence corresponding thereto. Applicants note that SEQ ID NO: 2 of '031 comprises 8 contiguous nucleobases of SEQ ID NOs: 12, 13, 31 and 32.

A second requirement of the amended claims is at least about 95% homology (as defined in the specification at page 14, lines 17-20) to SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34 or an RNA sequence corresponding thereto over the full length of the isolated oligonucleotide. As the Examiner notes in the Office Action, substantial homology is defined in the specification. At page 14, lines 17-20, it is disclosed that substantial homology is most preferably at least about 95% sequence identity over a defined length of the two molecules being aligned. When aligned with the oligonucleotides of the invention to take maximum advantage of the contiguous 8 nucleobase sequence of SEQ ID NO: 2 of '031 (as shown below), the only sequence identity between SEQ ID NO: 2 of '031 and the recited oligonucleotides is the 8 nucleobase sequence:

GTGTGAAGGGTTCATATGC	SEQ ID NO: 2 ('031)
CGCGCGGTGAAGGG	SEQ ID NO: 12 (Applicant)
GCGCGGTGAAGGG	SEQ ID NO: 13 (Applicant)
CCCGCGCGGTGAAGGGCGTC	SEQ ID NO: 31 (Applicant)
CCCCGCGCGGTGAAGGGC	SEQ ID NO: 32 (Applicant)

SEQ ID NO: 2 of '031 is therefore only 42% homologous to SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 31 and SEQ ID NO: 32 over its full length (i.e., 8 of 19 nucleobases). As SEQ ID NO: 2 does not meet the claim limitation of at least about 95% homology, Koster et al. does not anticipate the claims as amended and withdrawal of the rejection is requested.

Claims 25-28 and 32 are rejected under 35 USC §102(b) as allegedly anticipated by Stoler et al. (US Patent No. 5,912,147, hereinafter "'147"). The Examiner notes that SEQ ID NO: 15 of '147 contains an 8 nucleobase portion that is complementary to SEQ ID NO: 17 and SEQ ID NO: 21 as well as identical to SEQ ID NO: 32 of the instant invention. Complementarity to the recited sequences has been deleted from the amended claims, so the only relevant comparison is to SEQ ID NO: 32 of the claimed invention:

CGCGCGCGGT	SEQ ID NO: 15 ('147)
CCCCGCGCGGTGAAGGGC	SEQ ID NO: 32 (Applicant)

In spite of 9 identical nucleobases, the homology of SEQ ID NO: 15 of '147 to SEQ ID NO: 32 is only 90% (9 of 10 nucleobases). As SEQ ID NO: 15 does not meet the claim limitation of at least about 95% homology, Stoler et al. does not anticipate the invention as presently claimed. Withdrawal of the rejection is requested.

Rejection Under 35 USC §103(a)

Claims 25-28 and 30-32 are rejected under 35 USC §103(a) as allegedly unpatentable over either '031 or '147, in further view of Skerra, A. (Nucleic Acids Research, 1992, 20:3551-3554). The teachings of '031 and '147 relied upon in the rejection are discussed above. Skerra is relied upon for its teaching of introduction of a phosphorothioate bond in the oligonucleotide. It is asserted that it would have been obvious to make an oligonucleotide comprising 8 contiguous nucleobases which is substantially identical or complementary to at least a portion of SEQ ID NO: 21 of the present invention and to have the oligonucleotide further comprise a phosphorothioate internucleoside linkage as taught by Skerra.

The Examiner points out that SEQ ID NO: 2 of '031 is directed to a CFTR gene and that SEQ ID NO: 15 of '147 is directed to amplification of genomic DNA from tumors. The presently claimed oligonucleotides of the invention are directed to bcl-2 and therefore comprise at least 8 contiguous nucleobases found in certain oligonucleotides that are complementary to the bcl-2

sequence. One skilled in the art, given the sequences of '031 and '147 would not be motivated to extend their 8 contiguous nucleobase homology to make the claimed oligonucleotides because the added nucleobases would be expected to reduce the specificity of the oligonucleotides for their intended targets, i.e., CFTR and genomic DNA from tumors.

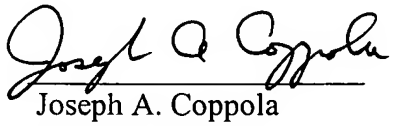
The addition of Skerra for its teaching of phosphorothioates does not overcome this deficiency in the primary references. It is therefore requested that the rejection be withdrawn.

Applicants note that prior art showing only the phosphorothioate linkages is relied upon in making the rejection under 35 USC §103(a), and the rejection of all claims is reasoned on the basis of this prior art. However, Claims 25-28 and Claim 32 do not recite a non-naturally occurring internucleotide linkage (Claim 30) or a phosphorothioate internucleotide linkage (Claim 31). It is not clear to Applicants how the Skerra reference relates to claims other than Claims 30 and 31, and it is respectfully submitted that the 35 USC §103(a) rejection as presented should properly be applied only to Claims 30 and 31.

Conclusions

In view of the foregoing amendments and remarks, Applicants respectfully submit that the present application is condition for allowance and an action passing this case to issue is requested. If the Examiner would like to discuss any remaining issues in this application, she is invited to contact the undersigned at the phone number provided below.

Respectfully submitted,

BY: 

Joseph A. Coppola
Reg. No. 38,413

KENYON & KENYON
One Broadway
New York, NY 10004
(212) 425-7200 (telephone)
(212) 425-5288 (facsimile)

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